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Social Determinants of Health Associated With the Development of Sepsis in Adults: A Scoping Review

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OBJECTIVE: Evaluating risk for sepsis is complicated due to limited understanding of how social determinants of health (SDoH) influence the occurence of the disease. This scoping review aims to identify gaps and summarize the existing literature on SDoH and the development of sepsis in adults.

DATA SOURCES: A literature search using key terms related to sepsis and SDoH was conducted using Medline and PubMed.

STUDY SELECTION: Studies were screened by title and abstract and then full text in duplicate. Articles were eligible for inclusion if they: 1) evaluated at least one SDoH on the development of sepsis, 2) participants were 18 years or older, and 3) the studies were written in English between January 1970 and January 2022. Systematic reviews, meta-analyses, editorials, letters, commentaries, and studies with nonhuman participants were excluded.

DATA EXTRACTION: Data were extracted in duplicate using a standardized data extraction form. Studies were grouped into five categories according to the SDoH they evaluated (race, socioeconomic status [SES], old age and frailty, health behaviors, and social support). The study characteristics, key outcomes related to incidence of sepsis, mortality, and summary statements were included in tables.

DATA SYNTHESIS: The search identified 637 abstracts, 20 of which were included after full-text screening. Studies evaluating SES, old age, frailty, and gender demonstrated an association between sepsis incidence and the SDoH. Studies that examined race demonstrated conflicting conclusions as to whether Black or White patients were at increased risk of sepsis. Overall, a major limitation of this analysis was the methodological heterogeneity between studies.

CONCLUSIONS: There is evidence to suggest that SDoH impacts sepsis incidence, particularly SES, gender, old age, and frailty. Future prospective cohort studies that use standardized methods to collect SDoH data, particularly race-based data, are needed to inform public health efforts to reduce the incidence of sepsis and help clinicians identify the populations most at risk.

KEY WORDS: critical care; prognostic; scoping review; sepsis; social determinants of health

Sepsis is the life-threatening host response to infection (1). In 2017, there was an estimated 48.9 million cases of sepsis globally, with a mortality rate of 30%, accounting for roughly 19.7% of all deaths (2, 3). It is also associated with an enormous financial cost, estimated to upward of $1 billion in 2018 and accounting for nearly 2% of all healthcare spending, in Ontario (4). Although we understand that access to health care affects mortality, less is known about the impacts of social determinants of health (SDoH), particularly in high-income settings.

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The World Health Organization defines SDoH as "the conditions in which people are born, grow, live, work, and age (5)." For centuries, poverty has been understood to be associated with poor health outcomes, but research over the past few decades has expanded this understanding to include additional factors such as race, education, social status, and levels of social support (6). A study analyzing national data from 2001 in the United States found that avoidable factors associated with low education status accounted for almost half of all deaths in adults (7). More recently, researchers have identified Black and South Asian individuals as being at a higher of COVID-19 infections and mortality, respectively (8, 9). However, these risks were partially attributable to socioeconomic status (SES), education, occupation, and housing status. Given that SDoH have been associated with the incidence and outcomes of multiple health conditions and, particularly, sepsis due to COVID-19, understanding the relationship between SDoH and sepsis is important. To date, there has not been a review summarizing the literature on SDoH and sepsis, despite the known importance.

The purpose of this scoping review is to address gaps in the current literature on the association between SDoH and the development of sepsis in adults. The current Surviving Sepsis Campaign provides guidelines for sepsis management but has no recommendations for identifying patients at higher risk for developing sepsis (10). Understanding the impact of SDoH on sepsis incidence would provide information on the most vulnerable populations and could alert healthcare professionals and guide clinical care. This may prove helpful given the current healthcare landscape, where many COVID-19 positive patients have died of sepsis, and the disproportionate impact on racialized communities (8, 9). Overall, understanding how SDoH influences sepsis development is important for directing public health and clinical efforts aimed at reducing health disparities.

MATERIALS AND METHODS

Protocol and Registration

The scoping review was conducted and reported in accordance with the criteria identified by the Preferred Reporting Items for Systematic review and Meta-analyses extension for Scoping Reviews guidelines (11). The study was a retrospective analysis of previously published literature, and therefore, approval from research ethics board was not needed. The protocol for this study was published in *BMJ Open* (12).

Search Strategy

A literature search was conducted using Medline and PubMed to identify primary studies that examined the effects of SDoH on the development of sepsis between January 1970 and January 2022. The search terms included a combination of key terms related to sepsis (sepsis odds ratio [OR] septicemia OR septic shock OR systemic infection OR bacteremia) and one of the defined SDoH. These SDoH included SES, race, substance-related disorders, social support levels (independent, living with family, or living in a long-term care facility), registration with a family doctor, mental illness, alcohol use, smoking status, frailty, and gender. Additionally, the reference lists of included research articles and published reviews were searched to identify other potentially eligible studies. The search was restricted to studies written in English and involving human participants. A sample search can be found in **Supplemental File 1** (**Appendix 1**, http://links.lww.com/CCX/B30).

Study Selection

Two reviewers (F.S., C.M.) independently evaluated all articles, first by title and abstract followed by full-text review. Disagreements were resolved by discussion with a third reviewer (A.E.F.-R.). Articles eligible for inclusion in the review met all the following criteria:

1) Studies examined the effect of at least one of the following SDoHs (i.e., SES, race, substance-related disorders, social support levels, registration with a family doctor, mental illness, alcohol use, smoking status, frailty, and gender) on the development of sepsis.
2) Study participants were adults 18 years or older.
3) Studies were written in English between January 1970 and January 2022.

Systematic reviews and meta-analyses, editorials, commentaries, letters, and studies with nonhuman participants were excluded.

Data Extraction

The relevant data were extracted by two reviewers (F.S., C.M.) from the included studies using a standardized data extraction form. The following data

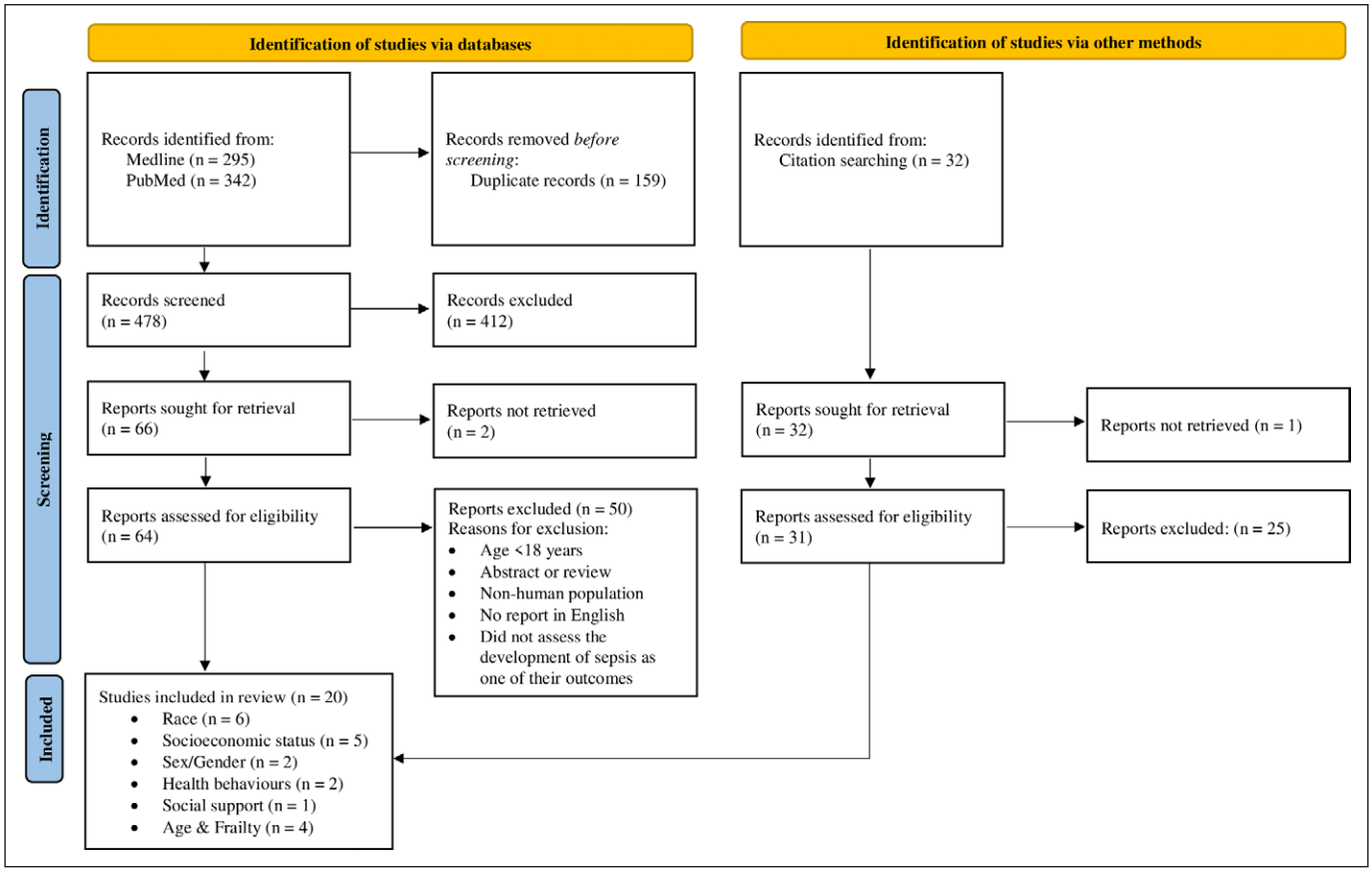

Figure 1. Flowchart of literature identification, review, and selection.

were extracted: study characteristics (year of publication and country of origin), study design, number of participants, results examined in each study, and a description of the key findings related to the effects of SDoH studied on the development of sepsis. Although risk of bias (RoB) assessments and quality assessments are not typically performed in scoping reviews (13), an analysis of the methodological quality of each study was performed using the appropriate Joanna Briggs Institute (JBI) critical appraisal checklist (12). This was done to determine the limitations of included studies and inform discussions on how future studies should be conducted.

Analysis

To guide the reporting of the results, the SDoH were grouped into the following categories: race, SES, old age and frailty, health behaviors (i.e., smoking status and alcohol use), and social support. Included studies were classified into the category they were most relevant to and synthesized within each of these categories. When studies reported similar findings, they were reported in parallel, whereas studies reporting contrasting results were compared, where appropriate. Given the purpose of a scoping review, no statistical analysis was performed (13).

The characteristics of the studies, including country of origin, methodology, sample size, and population, as well as key results related to the incidence of sepsis, of each included study were summarized in tables. Mortality outcomes and summary statements of overall key findings, as described by the study authors, were also included in tables.

RESULTS

Selection of Sources of Evidence

The search strategy yielded 637 abstracts, and 32 additional studies were identified through citation searching. Ninety-five articles were reviewed in full text, of which 75 studies were excluded (Figure 1). The remaining 20 were included in the review. A list of all included studies can be found in Supplemental File 1 (**Appendix 2**, http://links.lww.com/CCX/B30).

Characteristics of Source of Evidence

Of the 20 studies that met the inclusion criteria, there were 15 retrospective cohort, four prospective cohort, and one case-control study. Each study examined the relationship between sepsis and an SDoH (six race studies, five SES, four old age and frailty, two health behaviors, two gender, and one social support). No studies evaluating registration with a family doctor or mental illness as a social determinant for sepsis were identified. Studies were published between 2000 and 2019; however, the earliest enrollment of patients within studies began in 1979. Sixteen of the studies were conducted in the United States, whereas the remaining studies were conducted in Europe. Study size varied greatly between studies, with the smallest cohort of 327 patients and the largest cohort of nearly 1 million. The percentage of women in the study ranged from 21.0% to 58.1%. The study characteristics are presented in **Table 1**.

Critical Appraisal Within Sources of Evidence

The 19 cohort studies and one case-control were evaluated using the JBI checklist for their respective study types. Common methodological concerns were the study's exposure measurement, the identification of confounding variables, and strategies to address confounding variables. RoB analysis for each study with justification is found in Supplemental File 1 (**Appendix 3, Tables 1** and **2** and **Fig. 1,** http://links.lww.com/CCX/B30).

Race

Six cohort studies investigated the impact of race on the development of sepsis, and four identified a higher risk of sepsis development in Black patients compared with White patients (14–17) (**Table 2**). In contrast, two studies found that White patients had a higher incidence of sepsis compared with Black patients (18, 19). Fifty percent of the studies also investigated at least one non-White and non-Black population.

There were three studies that looked at the incidence of sepsis in non-White and non-Black patients, which had conflicting findings. The study including Asian patients found that they were most likely to develop post-traumatic sepsis (17). However, data on sepsis development in Hispanic patients were inconsistent. Compared with White and Black patients, studies reported both an increased and decreased risk of sepsis (14, 19). Additionally, the only study reporting non-White and non-Black patients in a single "Other" category found this group to have a higher relative risk than White patients, and a higher relative risk than Black patients (16). These findings suggest that the rates of sepsis development in other races may differ compared with White and Black patients, but existing data are sparse and conflicting.

Comparisons between these studies are limited by their different study periods (Table 2), as sepsis, definitions, epidemiology, and prognosis have changed over time (34). However, across all studies, Black patients with sepsis were younger than White patients, which is consistent with the lower age of the Black population in the United States (35, 36). Limitations include the varied methods of reporting the incidence, identification, and populations of sepsis in the included studies, limited data on patients who were not White or Black, and challenges associated with controlling for socioeconomic factors, lifestyle, biology, and race-based differences in access and quality of care, as reported by the included studies.

Socioeconomic Status

Five studies investigated the impact of SES on the development of sepsis, all indicating that low SES was significantly associated with a higher incidence of sepsis (20,22–24) (**Table 3**). Four studies continued to show an association between low SES and sepsis incidence after adjusting for confounding variables. One study adjusted for 20 confounding factors including sex, calendar year, and comorbidities, and still demonstrated that SES and sepsis incidence were inversely related (23). Additional SDoH may be integrated into SES. For example, differences in chronic diseases and substance abuse rates between the SES groups explained 43–48% of the differences in the risk of bacteremia (22), and comorbidities and surgical procedures were responsible for a significant portion of the association between SES and sepsis (23).

Although all studies indicated an increased risk of sepsis in lower income groups, the assessment of SES varied significantly. Measures of SES included the highest educational level achieved by the patient (23), composites of education and personal income (22),

TABLE 1.
Study Characteristics of All 20 Included Studies

Study	Methodology	Population	*n* (Total Population)	Age (Mean)[a]	% Female
Race					
Barnato et al (14)	Retrospective cohort	Non-HIV/AIDS hospitalizations in Florida, Massachusetts, New Jersey, New York, Virginia, and Texas	8,940,278	All ages (36.1)	NR
Dombrovskiy et al (15)	Retrospective cohort	Adult inpatients with sepsis in New Jersey	24,839	>18 yr	45.8
Esper et al (16)	Retrospective cohort	Sepsis hospitalizations in all nonfederal acute care hospitals	930,000,000	(60.5)	NR
Mayr et al (17)	Retrospective cohort	White or Black patients hospitalized for infection in Arizona, Florida, Massachusetts, Maryland, New Jersey, New York, and Texas	2,261,857	All ages	58.1
Moore et al (18)	Prospective cohort	Community-dwelling healthy adults at baseline	29,690	≥45 yr	55.1
Plurad et al (19)	Retrospective cohort	Patients admitted to the ICU due to trauma	3,998	(36.7)	21.0
Socioeconomic status					
Donnelly et al (20)	Prospective cohort	ED visits and hospitalizations across the United States	26,604	≥45 yr	55.0
Goodwin et al (21)	Retrospective cohort	Severe sepsis hospitalizations in South Carolina	24,395	≥ 20 yr	47.2
Koch et al (22)[a]	Case-control	Patients in North Denmark hospitalized with community-acquired bacteremia	45,287	30–65 yr	47.2
Oestergaard et al (23)[a]	Retrospective cohort	All Danish residents >30 yr old	3,394,936	≥ 30 yr	50.0
Mendu et al (24)	Retrospective cohort	Adults admitted to Brigham Women's hospital, or Massachusetts General Hospital	14,597	≥ 18 yr (62.3)	43.0
Health behaviors					
Ferro et al (25)	Retrospective cohort	Critically injured patients (Injury Severity Score ≥ 20) at single center in Arizona	327	18-65 yr	27.2
O'Brien et al (26)	Retrospective cohort	ICU admissions at single center Colorado	11,651	>18 yr	56.7
Frailty and age					
Mahalingam et al (27)	Retrospective cohort	Community-dwelling healthy adults at baseline	30,239	≥45 yr	53.2
Martin et al (28)	Longitudinal observational	Community-dwelling healthy adults at baseline	10,422,301	NR	NR
Wang et al (29)	Retrospective cohort	Community-dwelling healthy adults at baseline	30,239	NR	55.0
Angus et al (30)	Retrospective cohort	Acute care hospitalization in Florida, Maryland, Massachusetts, New Jersey, New York, Virginia, and Washington	6,621,559	63.8	50.4
Gender					
Sakr et al (31)[a]	Post hoc analysis of prospective cohort	Patients admitted to 24 Italian ICUs	3,902	>18 yr (64.3)	36.5
Wichmann et al (32)[a]	Prospective cohort	Surgical ICU patients single center Germany	4,218	NR	35.8
Social support					
Seymour et al (33)	Retrospective cohort	Hospital discharges from New Jersey	876,963	≥45 yr	51.7

ED, emergency department, NR = not reported.
[a]Studies conducted outside the United States.
Mean is provided in brackets.

TABLE 2.
Association of Race and Sepsis

Study	Data Source	Sepsis Identification	Primary Outcome(s)	Key Findings (Sepsis)	Key Finding (Mortality)	Summary Statement
Race ($n = 6$)						
Barnato et al (14)	U.S. Census and Hospital discharge dataset	Co-occurrence of ICD-9-CM codes for bacterial or fungal infections process and acute organ dysfunction	Severe sepsis	Incidence Black: 6.08/1,000 persons Hispanic: 4.06/1,000 persons White: 3.58/1,000 persons Black RR: 1.44 (95% CI, 1.42–1.46)	Case Fatality Rate Black: 26.1% White: 24.2% Hispanic: 24.6%	Black race is independently associated with higher severe sepsis incidence
Dombrovskiy et al (15)	New Jersey state inpatient database	Sepsis-3 consensus definitions	Sepsis hospitalization	Incidence White: 371.6 ± 2.69/100,000 persons Black: 846.4 ± 11.82/100,000 persons	Mortality (per 100,000, mean ± SE) Black: 208.6 ± 6.04 White: 99.6 ± 1.37	Rates of hospitalization for sepsis in Blacks is greater than in Whites, without differences in case fatality
Esper et al (16)	National hospital discharge database, including all nonfederal acute care hospitals	Sepsis-2 consensus definitions	Sepsis	RR (95 % CI) Black: 1.90 (1.82–1.98) Other: 1.85 (1.75–1.95)	NR	Blacks have a greater frequency of Gram-positive infections independent of the infection source
Mayr et al (17)	State hospital discharge databases of seven U.S. states	ICD-9-CM codes	Infection and severe sepsis	Incidence Black: 9.4/1,000 persons White: 5.6/1,000 persons	Mortality odds ratio, adjusted Black: 1.8 White: 1.0	Higher likelihood of being hospitalized with infection in Black patients compared with White patients
Moore et al (18)	The Reasons for Geographic and Racial Differences in Stroke cohort and medical records for specific health events	Sepsis-2 consensus definitions	First-infection or first-sepsis event	Incidence ratio Black: 6.93/1,000 PYs White: 9.10/1,000 PYs	NR	Black participants are less likely than White participants to experience infection and sepsis events
Plurad et al (19)	ICU database	Infection + any of the four following: temp > 38, heart rate > 90, Respiratory rate > 20, WBC > 12, or vasopressor requirement	Development of post-traumatic sepsis	% Incidence of sepsis Asian: 23.7% Blacks: 15.3% Hispanic: 16.1% White: 17%	% Mortality Asian: 37.1% Blacks: 25.4% Hispanic: 38.6% White: 37%	Race is independently associated with increased risk of post-traumatic sepsis and may be related to sepsis-related mortality

ICD-9 = *International Classification of Diseases,* Ninth Edition, ICD-9-CM = *International Classification of Disease,* Ninth Revision, Clinical Modification, NR = not reported, PYs = person years, RR = risk ratio.

TABLE 3.
Association of Socioeconomic Status and Sepsis

Study	Data Source	Sepsis Identification	Primary Outcome(s)	Key Findings (Sepsis)	Key Finding (Mortality)	Summary Statement
SES ($n = 5$)						
Donnelly et al (20)	The Reasons for Geographic and Racial Differences in Stroke cohort, medical records & 2000 census	Sepsis-2 consensus definitions	Infection or sepsis	Incidence ratio, SES quartiles Q1: 9.1 (8.2–10.1)/1,000 PYs Q4: 6.3 (5.6–7.9)/10,000 PYs OR Q4 (crude): 0.84 (0.66–1.06) Q4 (adjusted): 0.90 (0.67–1.21)	NR	Participants in low SES neighborhoods have higher rates of infection, but no difference in odds of sepsis at presentation
Goodwin et al (21)	U.S. Census database, South Carolina (SC) hospital discharge database, SC Department of Health and Environmental Control	ICD-9-CM codes	Sepsis	Incidence MUAs: 8.6/1,000 persons Non-MUAs: 6.8/1,000 persons	Mortality OR (95% CI), adjusted MUA: 1.12 (1.04–1.20)	Residence in MUA is associated with higher incidence rates of severe sepsis and higher odds of sepsis-related mortality
Koch et al (22)	Danish civil registration system	Cases identified from population-based bacteremia research database established by the Danish Collaborative Bacteremia Network	Community-acquired bacteremia	OR, adjusted, 95% CI Education: 1.60 (1.45–1.77) Income: 1.69 (1.54–1.86)	NR	Persons of lower SES, based on either education or income, are at increased risk of hospitalization for community-acquired bacteremia
Oestergaard et al (23)]	The Danish Civil Registration System, The Population Education Registry & Income Statistics Registry for adults >30 yr old	Microbiologically verified ICD-10-CM codes	SAB	N/A	NR	Declining levels of SES are associated with an increased risk of microbiologically verified SAB
Mendu et al (24)	Research Patient Data Repository (Brigham and Women's hospital & Massachusetts General hospital)	ICD-9-CM codes	Bloodstream infection 48 hours before or after critical care initiation	N/A	NR	There is an increase in risk of bloodstream infections near critical care initiation with increasing neighborhood poverty rate

ICD-9-CM = *International Classification of Diseases,* Ninth Edition, Clinical Modification, MUA = medically underserved area, NR = not reported, OR = odds ratio, PYs = person years, SAB = *Staphylococcus aureus* bacteremia, SES = socioeconomic status.

and whether a patient lived in a "medically underserved area" (21). Despite these differences, the overall findings suggest an association between low SES status and the risk of sepsis.

Old Age and Frailty

Four studies investigating the effect of age and frailty on sepsis were included in this review. These studies focused on related but distinct primary independent variables, including age, frailty, and chronic medical conditions (27–29).

In all studies reporting on age and chronic medical conditions, the incidence of sepsis increased with age (28–30). Martin et al (28) noted that the incidence of sepsis "increased exponentially in all age deciles." When examining the effects of chronic medical conditions, all 11 included conditions increased the risk of sepsis; however, chronic lung disease had the strongest adjusted and unadjusted association (29). Similarly, an increased incidence of sepsis was reported in frail patients, following adjustment for age, sex, obesity, and other comorbidities (27). Together, these studies demonstrate that age, frailty, and chronic medical conditions are independently associated with an increased risk of sepsis (**Table 4**).

Although all studies evaluated different primary outcomes, the analysis of these three variables together is important, as the prevalence of frailty, which is associated with increased morbidity and mortality (21), increases with age, contributing to a higher risk of sepsis among older adults (37). To date, no studies have evaluated their intersectionality and how they can jointly affect the incidence of sepsis.

Social Support

Only one study examining the effects of social support on sepsis incidence was identified (33). Specifically, Seymour et al. compared the incidence rate ratio (IRR) between widowed, divorced, single and married individuals and found that the incidence of sepsis increased in widowed, divorced, and single people (Table 4). These results persisted after adjustment for age, sex, and ethnicity. Multiple independent data sources were used to derive IRR, and there was no analysis of neighborhood or community factors related to marital status. This is of particular concern as previous studies (21) have identified neighborhood SES as a risk factor for sepsis, suggesting that other neighborhood-associated factors may also be important to consider.

Health Behaviors

Two studies investigating the impact of tobacco use and alcohol dependence on sepsis incidence were included in this review (25, 26). Although no differences in the incidence of sepsis were reported between tobacco users and nonusers, a significant association was identified between alcohol dependence and the incidence of sepsis and septic shock (**Table 5**). Both tobacco use and alcohol dependence have previously been studied in relation to sepsis (38, 39). In particular, the relationship between alcohol dependence and sepsis reported in the included study is consistent with the existing literature; however, the lack of clinical significance observed between smoking status and sepsis is contradictory (38). This may be due to limited sample size and inconsistent recording of patient smoking status. Although the results of the included studies vary, the results provide insight into how SDoH can affect sepsis incidence and a rationale for further exploration of health behaviors, including other substance use disorders.

Gender

Two studies investigated the impact of gender on sepsis in patients in the intensive care unit. Significantly more men developed sepsis compared with women (31, 32) (Table 5). The consistent findings of these studies and their large sample sizes (Table 5) suggest that differences in the occurrence of sepsis can be affected by gender. Both studies were limited by the use of retrospective data, and neither study analyzed the degree to which differences in behavior versus differences in biology mediate disparities or attempted to adjust for health behaviors, such as alcohol use, which can vary between men and women (40). Additionally, no existing literature has investigated how gender identity could impact sepsis independent of biological sex.

DISCUSSION

Overall, there is evidence that SDoH affects the incidence of sepsis. Studies evaluating SES, aging, frailty, gender, alcohol dependence, and social support demonstrated an association between sepsis and SDoH;

TABLE 4.
Association of Frailty, Age, Social Support, and Sepsis

Study	Data Source	Sepsis Identification	Primary Outcome(s)	Key Findings (Sepsis)	Key Finding (Mortality)	Summary Statement
Frailty and old age ($n = 4$)						
Mahalingam et al (27)	REGARDS cohort of community-dwelling adults	Sepsis-2 consensus definitions	First hospitalization for sepsis	Incidence ratio, frail vs nonfrail 15.5 (14.2–16.9)/1,000 PYs 6.6 (6.2–7.0)/1,000 PYs Adjusted HR: 1.44 (1.26–1.64)	30-d case fatality OR, frail vs nonfrail, adjusted: 1.62 (1.06–2.50)	Frailty was associated with increased long-term risk of sepsis and sepsis 30-day case fatality rate
Martin et al (28)	REGARDS cohort of community-dwelling adults	ICD-9-CM codes	Sepsis	Incidence, age 18–29: 29.6/100 000 persons 90–99: 2,422.3/100,000 persons Risk ratio > 65 yr: 13.1 (12.6–13.6)	Mortality, OR adjusted, >65: 2.26 (2.17–2.36)	Incidence of sepsis is disproportionately increased in elderly adults, and age is an independent predictor of mortality
Wang et al (29)	REGARDS cohort of community-dwelling adults	Sepsis-2 consensus definition	Sepsis	HR (95% CI), age 55–64: 1.44 (1.04–2.00) 65–74: 2.29 (1.66–3.16) 75+: 3.87 (2.805.35) Adjusted HR (95% CI), chronic medical condition Chronic lung disease: 2.43 (2.05–2.86) Peripheral artery disease: 2.16 (1.58–2.95) Chronic kidney disease: 1.99 (1.73 –2.29)	Not reported	Individuals with chronic medical conditions are at increased risk of developing future sepsis events
Angus et al (30)	U.S. Census and Hospital discharge dataset	Co-occurrence of ICD-9-CM codes for bacterial or fungal infections process and acute organ dysfunction	Severe sepsis	Incidence, age 5–14 yr: 0.2/1,000 60–64 yr: 5.3/1,000 ≥ 85 yr: 26.2/1,000	Mortality % Children: 10 ≥ 85 yr: 38.4	Incidence of sepsis is disproportionately increased in older adults, and age is associated with increased mortality

(*Continued*)

TABLE 4. (*Continued*).
Association of Frailty, Age, Social Support, and Sepsis

Study	Data Source	Sepsis Identification	Primary Outcome(s)	Key Findings (Sepsis)	Key Finding (Mortality)	Summary Statement
Social support ($n = 1$)						
Seymour et al (33)	Population-based cohort of hospital discharge data from New Jersey using the Healthcare Cost and Utilization Project 2006 State Inpatient Database	ICD-9-CM codes	Sepsis	Incidence rate ratio (95% CI) Widowed: 1.38 (1.17–1.63) Single: 3.5 (3.1–3.9) Legally separated: 1.5 (1.2–1.8)	Mortality, OR (95% CI), adjusted Women Married: 0.95(0.87–1.03) Divorced: 0.90 (0.74–1.09) Widowed: 1.0 (0.93–1.08) Single: 1.16 (1.03–1.3) Legally separated: 0.96 (0.73–1.26) Men Married: 1.0 (Ref) Divorced: 1.19 (1.03–1.40) Widowed: 1.0 (0.91–1.10) Single: 0.78 (0.73–0.85) Legally separated: 0.89 (0.68–1.17)	Hospitalization for sepsis is more common in single, widowed, and legally separated individuals compared with married individuals

HR = hazard ratio, ICD-9 = *International Classification of Diseases,* Ninth Edition, ICD-9-CM = *International Classification of Disease,* Ninth Revision, Clinical Modification, OR = odds ratio, PYs, person years, REGARDS = Reasons for Geographic and Racial Differences in Stroke.

TABLE 5.
Association of Health Behaviors, Gender, and Sepsis

Study	Data Source	Sepsis Identification	Primary Outcome(s)	Key Findings (Sepsis)	Key Finding (Mortality)	Summary Statement
Health behaviors ($n = 2$)						
Ferro et al (25)	Trauma registry	Sepsis-1 consensus definition	Sepsis	No difference in frequency of SIRS, sepsis, or septic shock SIRS $p = 0.606$ Sepsis $p = 0.738$ Septic shock $p = 0.656$	Not reported	Tobacco users do not have a higher incidence of pneumonia or sepsis
O'Brien et al (26)	The University Health System Consortium Clinical Database	*International Classification of Diseases,* Ninth Edition CM codes	Sepsis or septic shock	OR, adjusted, alcohol dependence Sepsis: 1.54 (1.25–1.91) Septic shock: 1.46 (1.01–2.11)	Mortality, OR (95% CI), alcohol dependence: 1.46 (1.01–2.11)	Alcohol dependence was independently associated with sepsis, septic shock, and hospital mortality
Gender ($n = 2$)						
Sakr et al (31)	Patients >18 admitted to the ICU	Sepsis-1 consensus definition	Sepsis in the ICU	Frequency of sepsis Women: 6.0% Men: 8.9% Severe sepsis within 48 h of admission Women: 2.3% Men: 4%	Mortality Women: 63.5% Men: 46.4%	Frequency of severe sepsis was lower in women than in men, but female gender was independently associated with a higher risk of death in the ICU due to severe sepsis
Wichmann et al (32)	Surgical ICU patient database	Not mentioned	Severe sepsis	Frequency of sepsis/septic shock Women: 7.6% Men: 10.4%	Mortality Women: 64.9% Men: 65.7%	Severe sepsis/septic shock incidence was lower in female ICU patients than in male ICU patients; however, sepsis-related mortality was not affected by gender

ICD-9-CM = *International Classification of Disease,* Ninth Revision, Clinical Modification, OR = odds ratio, SIRS = systematic inflammatory response syndrome.

however, the strength of the association varied. Race, the SDoH most studied, had four studies that showed an increased incidence of sepsis in Black patients compared with White, whereas two showed the opposite association. Ultimately, the conclusions are limited by the heterogeneity of the studies and their definitions of their respective SDoH, which provides insight into the need for future standardized definitions and collection of SDoH data.

SDoH are becoming an important focus in understanding how to effectively prevent acute and chronic conditions. During the COVID-19 pandemic, researchers evaluated how SDoH impacts rates of infection, hospitalization, and mortality (8). A study evaluating more than 23 million individuals identified that South Asian and Black patients were at higher risk of COVID-19 mortality compared with White patients. This difference remained significant after adjustment for confounding factors but was partially attributable to comorbidities and deprivation, a term that includes SES, education, occupation, and housing status. Other studies found that although Black and White patients had different risks of COVID-19 infections, this risk was mediated by community-level deprivation, especially for Black patients (8, 9). These studies highlight the importance of SDoH in understanding the disproportionate risk of COVID-19 experienced by various racial groups. Similarly, previous research has demonstrated that a greater number of SDoH is associated with a greater incidence of chronic diseases, such as stroke, as well as cancer mortality (41, 42). In our review, studies evaluating race had conflicting results, whereas studies evaluating SDoH, such as lower SES and poor social support, were associated with an increased incidence of sepsis. In line with COVID-19 findings and studies of other diseases, these results underscore the importance of collecting data on SDoH, including race, and highlight the need for a standardized approach to collecting sociodemographic and specifically race-based data (43).

This review highlights the importance of SDoH as risk factors for sepsis; however, they must be interpreted along with the heterogeneity of the study methodology and the results. Methodological heterogeneity between studies was due to differences in investigated populations, SDoH definitions, outcome measures, and the use of hospital discharge data to identify sepsis cases, which has a limited sensitivity for sepsis identification of 27.6–42.6% (41). Homogeneity in study location, with most conducted in the United States, limits the generalizability of these findings. Finally, although most studies adjusted for confounding variables, few analyzed how one SDoH could modify another. For our review specifically, included articles failed to account for SES as a confounding factor for the association between race and incidence of sepsis. This is particularly important given SES's strong association with incidence of sepsis, whereas race's association varied between studies. Overall, this review demonstrates a need for an intersectional approach that evaluates the cumulative impact of SDoH on sepsis incidence.

Despite these limitations, there were several strengths to our review. To our knowledge, this is the first review to evaluate any associations between SDoH and the development of sepsis in adults. Further, this study evaluated the quality of literature using the JBI checklist, providing organized insight into the strengths and limitations of individual articles. In addition, this review identified many gaps in the literature surrounding SDoH and sepsis.

Given that SDoH has been implicated in the progression and development of many health conditions (42, 44, 45), including sepsis, understanding both their independent and combined effects is important for improving sepsis prognosis. To address the heterogeneity of the existing studies, future prospective studies need to implement appropriate methods of collecting SDoH data, particularly race-based data. Current research data collection often conflates race-based terminology with ethnicity-based terminology (i.e., White vs Hispanic), failing to account for important differences between race and ethnicity. Although for the purposes of this review, the language was based on the included reviews, creating that standardized terms in the future will allow for an appropriate analysis of the effects of SDoH on the incidence of sepsis by ensuring comparability between studies. Further, this requires more prospective studies to understand the interactions between SDoH and sepsis. This will help guide the development of risk stratification models, as well as the clinical and policy-based interventions needed to improve sepsis diagnosis and prognosis. Identifying vulnerable populations with higher incidence of sepsis may allow SDoH to act as risk-assessment tools for

sepsis in the emergency department, helping to identify and guide early therapeutic intervention.

CONCLUSIONS

This scoping review is the first to evaluate SDoH in association with the development of sepsis. Studies evaluating SES, aging, frailty, and gender unanimously demonstrated an association between sepsis and SDoH. Further, studies examining other SDoH, particularly race, demonstrated heterogeneity in what populations are at greatest risk of developing sepsis. These heterogeneous results can be attributed to the different outcomes assessed, the methodology for collecting SDoH data, and the different populations investigated. Future prospective cohort studies are needed to reduce the methodological heterogeneity in SDoH reporting and increase the comparability of the studies. Given the high mortality rate of sepsis (2), there is an urgent need to use SDoH in conjunction with biological markers as risk stratification tools for improved disease management.

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Ms. Sheikh and Ms. Machon contributed to the conception and design of this scoping review and performed the literature screening. Ms. Sheikh, Ms. Catenacci, and Ms. Machon extracted the data and performed the risk of bias analysis. Ms. Sheikh and Mr. Douglas interpreted and synthesized the data, and Ms. Sheikh, Mr. Douglas, and Ms. Catenacci drafted the article. Ms. Sheikh, Mr. Douglas, Ms. Catenacci, and Dr. Fox-Robichaud provided a critical assessment of the article. All authors read and approved the final article.

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